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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/772,913	02/05/2004	Steven W. Dow	86715.0002	5237

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EXAMINER	
WEHBE, ANNE MARIE SABRINA	

ART UNIT	PAPER NUMBER
1633	

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09/19/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/772,913	DOW ET AL.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17,24-31,53 and 68-74* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17,24-31,53 and 68-74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/25/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and response received on 6/25/08 has been entered. Claims 1-16, 18-23, 32-52, and 54-67 have been canceled and new claims 68-74 have been added. Claims 17, 24-31, 53, and 68-74 are currently pending and under examination in the instant application. An action on the merits follows.

Those sections of Title 35, US code, not included in this action can be found in the previous office action.

Information Disclosure Statement

The information disclosure statement (IDS) filed 6/25/08 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered. Note that the U.S. Patents and U.S. Patent Application Publications listed in the IDS have been considered as indicated on the attached 1449. However, the more than 38 pages of foreign patent documents and non-patent literature citations have not been considered as the applicant has not provided any of the literally hundreds of references cited therein for consideration by the examiner. It is noted that the applicant states that copies of these references may be found in one or more of a number of unrelated U.S. Patent

Applications filed by unrelated inventors, such as statement does not comply with the requirements of 37 CFR 1.98. 37 CFR 1.98 (d)(1) states that a copy of any patent, publication, pending U.S. application or other information, as specified in paragraph (a) of this section, listed in an information disclosure statement is required to be provided, even if the patent, publication, pending U.S. application or other information was previously submitted to, or cited by, the Office in an earlier application, unless: (1) the earlier application is properly identified in the information disclosure statement and is relied on for an earlier effective filing date under 35 U.S.C. 120.

Claim Rejections - 35 USC § 112

The rejection of claims 66-67 under 35 U.S.C. 112, second paragraph, for indefiniteness is withdrawn in view of the cancellation of these claims.

Claim Rejections - 35 USC § 103

Amended and new claims 17, 24-31, 53, and 68-74 stand rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,589,466 (1996), hereafter referred to as Felgner et al., in view of U.S. Patent No. 6,670,186 (2003), hereafter referred to as Nair et al., and U.S. Patent No. 6,977,073 (2005), hereafter referred to as Cezayirli et al. Applicant's arguments have been fully considered but have not been found persuasive in overcoming the rejection for reasons of record as discussed in detail below.

The rejection of record is reiterated below for clarity in view of the addition of new claims 68-74, and is followed by the response to applicant's arguments.

Felgner et al. teaches methods of immunizing a mammal by administering a preparation comprising a cationic liposome containing an mRNA encoding an immunogenic peptide, wherein the expression of the immunogen in the cells of a mammal induces immune responses, including humoral and cellular immune responses, including cytotoxic T lymphocytes (CTL) (Felgner et al., columns 7-9, 20-22, 25-26, and 29-32, especially columns 8-9, bridging paragraph, and examples 7-9). In particular, Felgner et al. teaches that the immunogenic peptide is associated with a tumor and induces CTL capable of killing the tumor (Felgner et al., column 8). Felgner et al. further teaches that the preparation can include a nucleic acid encoding a cytokine, and preferably one of the interferons (Felgner et al., column 8 and columns 22-23, bridging paragraph). Felgner et al. also teaches that cationic liposomes can be unilamellar or multilammelar, formed from cationic lipids such as DOTMA, or DOTAP, and other materials such as cholesterol (Felgner et al., columns 25-26). In addition, Felgner et al. teaches that routes of administration of the peptide include intravenous administration and administration to a body cavity (Felgner et al., column 7, and column 32- example 9 for intravenous administration of mRNA/liposomes). Felgner et al. also teaches the inclusion of nonionic materials such as sugars in the preparations (Felgner et al., columns 23, and 32). Felgner et al. further teaches that the ratio of mRNA to liposome can vary, and exemplifies one ratio of 1:40 mRNA to cationic liposomes (Felgner et al., column 30).

Felgner et al. differs from the instant invention by teaching the use of a single mRNA immunogen associated with a tumor instead of total tumor RNA or total tumor mRNA. Nair et

al. supplements Felgner et al. by teaching RNA/cationic liposome compositions useful for transfecting cells in order to stimulate immune responses where the RNA is total RNA or polyA+RNA derived from a tumor, i.e. mRNA (Nair et al., columns 1-5, especially column 5). Nair et al. provides motivation for using total tumor RNA and especially total tumor mRNA by teaching that the use of RNA enriched tumor preparations circumvents the need to isolate and identify a tumor antigen, has the capacity to elicit immune responses against multiple tumor antigens, thus reducing escape mutants, and extends the immunotherapy methods to tumors in which specific tumor antigens have not been identified (Nair et al., columns 1 and 6). Nair et al. further teaches that the RNA can be derived from tumors such as melanomas, breast cancer, prostate cancer, bladder cancer, pancreatic cancer, colon cancer, and ovarian cancer (Nair et al., column 3). Cezayirli et al. further supplements the teachings of Felgner et al. and Nair et al. by teachings that in order to induce multivalent vaccination against cancers such as lung cancer, antigen presenting cells such as dendritic cells can be contacted with a representative sample of different allogeneic tumor RNAs, such as the combination of tumor RNAs from progressive stages of the same cancer type (Cezayirli et al., columns 4-6). Cezayirli et al. further provides motivation for using a plurality of RNAs from tumor of the same histological type by teaching that by using a combination of RNAs representing various differentiation periods in the disease state progression a vaccine can be produced that may protect against a whole spectrum of a specified cancer (Cezayirli et al., column 4, lines 44-67).

Thus, based on the motivation provided by Nair et al. for using total tumor RNA or total tumor mRNA over isolated RNA encoding a tumor antigen in methods to stimulate anti-tumor immune responses, it would have been *prima facie* obvious to the skilled artisan at the time of

filing to utilize total tumor RNA or mRNA derived from tumors such as melanomas, lung or colon carcinomas instead of a single mRNA encoding a tumor antigen in the methods of stimulating immune responses in a mammal taught by Felgner et al. In addition, based on the motivation to combine RNAs from different stages of a tumor type in order to vaccinate against a spectrum of differentiation states of a cancer, it would have been *prima facie* obvious to the skilled artisan at the time of filing to utilize a mixture of total tumor RNAs from allogeneic tumors of a specified type in different stages of differentiation instead of a single mRNA or total tumor RNA from a single tumor cell in the methods of stimulating immune responses in a mammal taught by Felgner et al. Further, the skilled artisan would have had a reasonable expectation of success in using total tumor RNA or total tumor mRNA and cationic liposomes to generate anti-tumor immune responses in view of the successful use by Felgner of mRNA/cationic liposomes to induce immune responses when administered intravenously and the successful use by Nair et al. of total tumor RNA/cationic liposomes to transfect cells.

The applicant argues that neither Nair et al. nor Cezayirli et al. are pertinent references since they were filed after the effective filing date of the instant application and that it is possible that teachings in each patent are not supported by parent applications or provisional applications. In response, the applicant has provided no evidence that either of Nair et al. or Cezayirli et al. are not entitled to benefit of priority to the parent applications and provisional applications listed on the face of each patent. Cezayirli et al. claims benefit as a continuation, not a continuation in part, to several non-provisional parent U.S. applications dating back to at least February 1998. While Cezayirli et al. further claims benefit to provisional applications filed in 1997, the claim for benefit to various non-provisional parent applications is enough to clearly establish that

Cezayirli et al. is a valid reference. The parent applications and the Cezayirli Patent have identical specifications and thus provide the same teachings as set forth in the rejection of record. Therefore, Cezayirli et al. clearly qualifies as prior art under 35 U.S.C. 102(e). Nair et al. also clearly qualifies as prior under 35 U.S.C. 102(e). While it is true that Nair et al. claims benefit of priority as a continuation-in-part of several non-provisional U.S. Patent applications, the specifications of these parent applications supports the teachings cited in Nair et al. For example, parent application 09/171,916, filed April 30,1997, and issued as U.S. Patent 7,105,157, provides the same teachings as Nair et al., see especially columns 4-5 of the 7,105,157 patent. Likewise, parent applications 09/073,819, filed May 6, 1998, and issued as U.S. Patent 6,306,388, and 08/640,444, filed on April 30, 1996, and issued as U.S. Patent 5,853,719, all disclose the same teachings as Nair et al., see columns 1-4. Thus, applicant's arguments are not persuasive as both Nair et al. and Cezayirli et al. are entitled to benefit of priority prior to the effective filing date of the instant application.

Applicant's also references their earlier arguments regarding the teachings of Felgner et al. and Nair et al. However, these arguments were addressed in full in the previous office action and were not found persuasive.

No claims are allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all official communications, **the new technology center fax number is (571) 273-8300**. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197.

Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

/Anne Marie S. Wehbé/
Primary Examiner, A.U. 1633